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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,284	02/07/2005	Gesine Schliecker	I-2002.001 US	5686
31846 7590 06/29/2010 Intervet/Schering-Plough Animal Health Patent Dept. K-6-1, 1990 2000 Galloping Hill Road Kenilworth, NJ 07033-0530			EXAMINER PERREIRA, MELISSA JEAN	
			ART UNIT 1618	PAPER NUMBER
			NOTIFICATION DATE 06/29/2010	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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patents@spcorp.com

Office Action Summary	Application No. 10/501,284	Applicant(s) SCHLIECKER ET AL.	
	Examiner MELISSA PERREIRA	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 and 21-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 21-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/24/10 has been entered.

Claims and Previous Rejection/Objection Status

2. Claims 1-19 and 21-26 are pending in the application.
3. The rejection of claims 1-19 and 21-26 under 35 U.S.C. 103(a) as being unpatentable over Krone et al. (US 5,391,696) in view of Lewis (US 5,838,571) and in further view of Suzuki et al. (US 6,015,789) and Remington's Pharmaceutical Sciences 1990 18th Ed. Chpt. 89 is modified.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-19 and 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krone et al. (US 5,391,696) in view of Suzuki et al. (US 6,015,789)

and in further view of Remington's Pharmaceutical Sciences **1990** 18th Ed. Chpt. 89 and Lewis (US 5,838,571).

6. Krone et al. (US 5,391,696) discloses formulations comprising a.) polytartrate polymer, such as (2',3'-(1',4'-diethyl)-L-tartyl poly-(2,3-O-isopropylidene)-L-tartrate); b.) buserelin; c.) polyethylene glycol and d.) pharmaceutically acceptable excipients, etc. (abstract; column 10, lines 36-45 and 54-59). The formulations of the disclosure may be formed via compaction/compression and do not comprise a barrier structure (abstract; column 1, lines 9-14; column 2, lines 21-27; column 11, lines 35-40).

7. Krone et al. teaches that the polytartrate preparations have a decreased "initial burst" which implies that there is a second release of active agent (column 2, lines 21-25). The release rate of the "secondary burst" of the instant claims is defined as occurring over 2-4 days in the specification (specification p15, lines 10-12) and therefore the second release of active agent of Krone et al. encompasses the "secondary burst" of the instant claims as it may be a prolonged release.

8. In regards to the "lag time" the specification recites (p13, lines 17-20 and 30-33), "a secondary "lag phase" of **low or no** release of the drug followed by a second burst". Therefore, the polytartrate tablet formulations which are prepared via compaction/compression of Krone et al. encompass the composition of the instant claims as they have a first "initial burst", an implied second release of active agent (burst) and the phase between the bursts (i.e. lag phase) which may release drug. Therefore, the time between bursts of the polytartrate formulations of Krone et al. encompass the "lag phase" of the instant claims.

Art Unit: 1618

9. Also, the recitation, “determining a time of the lag phase”, is a mental step and does not contain any active technique (manual steps) for determining a time of the lag phase. There are no specific active steps to define how such determining is performed or which limit the amount of time of the lag phase.

10. Krone et al. does not disclose the GnRH agonist nafarelin, the method of administering the pharmaceutical composition or the process for preparing the pharmaceutical composition of the instant claims.

11. Suzuki et al. (US 6,015,789) discloses a pharmaceutical composition/solid tablet preparation comprising a GnRH agonist, such as buserelin or nafarelin; pharmacologically acceptable carrier; etc. for administration to a human being to treat sex hormone-dependent disease (claims 1,2; column 97, lines 63-66; claim 2; column 98, lines 17-25; column 101; column 102, lines 45-55). The pharmaceutical composition/solid tablet preparation comprising excipients (i.e. polyethylene glycol) are prepared via compression (column 99, lines 23-33).

12. Remington's Pharmaceutical Sciences **1990** 18th Ed. Chpt. 89 discloses the preparation of oral solid dosage forms from granulation techniques which involve mixing the materials, sieving the mixture and shaping the mixture with tableting equipment (especially see p1634; methods of preparation p1641-1646).

13. Lewis (US 5,838,571) discloses that standard tablet compression force of a conventional tablet is in the range of 18 to 27 kN (column 13, lines 1-7).

14. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute one GnRH agonist, such as buserelin of Krone et al. for an

Art Unit: 1618

equivalent GnRH agonist, such as nafarelin of Suzuki et al. in the polytartrate solid tablets (prepared via compression) of Krone et al. as it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect, such as treat a sex hormone-dependent disease. Suzuki et al. teaches of the administration of nafarelin or buserelin preparations to humans and therefore it would have been obvious to one skilled in the art to administer a polytartrate composition comprising nafarelin or buserelin to a human for the controlled release of the nafarelin to treat a sex hormone-dependent disease.

15. Remington's pharmaceutical sciences teaches of standard oral tablet formation involving mixing the components of the composition, sieving and compressing with tableting equipment and therefore it would have been obvious to one skilled in the art to use these standard techniques of Remington's for the preparation of the polytartrate composition of Krone et al.

16. The standard compression force for the preparation of a conventional tablet is in the range of 18 to 27 kN as taught by Lewis and therefore the polytartrate solid tablets (prepared via compression), which do not comprise a barrier structure, of Krone et al. encompass the composition of the instant claims which is prepared via compression with a compression force from 10 to 65 kN/cm². The simple compression of polytartrate compositions provides for release of the pharmaceutically active material in a pulsatile manner as evidenced by the specification (specification p3, lines 28-33). Krone et al.

Art Unit: 1618

does not explicitly teach that the tablets are pulsatile but teaches that the polytartrate composition are prepared via compression and have a decreased "initial burst" which shows that they provide an initial burst and thus are pulsatile to a degree.

17. The formulation of the combined disclosures encompasses the composition of the instant claims and is capable of the same functions, such as forming degradation products that increase the pressure inside the composition, capable of releasing the pharmaceutically active material in a pulsatile or triphasic manner, etc. and has the same properties, such as a glass transition temperature that is greater than 40°C.

Therefore, the burden is shifted to applicant to show that the pharmaceutical composition of the instant claims is materially different than the polytartrate polymer formulation of Krone et al.

18. It is respectfully pointed out that instant claims 1-13 and 22-23 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Response to Arguments

19. Applicant's arguments filed 5/24/10 have been fully considered but they are not persuasive.

Art Unit: 1618

20. Applicant asserts that an “initial burst” does not require or imply a second or subsequent burst. The “initial burst,” as would be understood by one of ordinary skill in the art at the time of the invention, refers only to the increased release rate upon initial administration until the preparation settles into its normal release rate.

21. The polytartrate preparations of Krone et al. have an “initial burst” which implies a second release of active agent. The specification states that the release rate of the “secondary burst” of the instant claims occurs over 2-4 days (specification p15, lines 10-12) and therefore the second release of active agent of Krone et al. encompasses the “secondary burst” of the instant claims as it may be a prolonged release.

22. Applicant asserts that the office appears to be improperly conflating the term “burst” with the steady state release. As would be understood by one of ordinary skill in the art at the time of the invention, a “burst” is a release of pharmaceutical over and above the steady state release. Thus, the steady state release rate/moderate release taught by Krone et al. is not a “burst”.

23. The specification states that the release rate of the “secondary burst” of the instant claims occurs over 2-4 days (specification p15, lines 10-12) and therefore the second release of active agent of Krone et al. encompasses the “secondary burst” of the instant claims as it may be a prolonged release.

24. Applicant asserts that Krone et al. teaches that the “initial burst” is unwanted and thus teaches away from the claimed compositions. Consequently, the applicants submit that the references do not teach or suggest a pulsatile release, including an initial burst, a lag phase, and thereafter a second burst of a pharmaceutically active material.

Art Unit: 1618

25. Krone et al. teaches that the polytartrate preparations do have an “initial burst” and albeit a decreased “initial burst” and therefore does not teach away from compositions with an “initial burst”. The “initial burst” implies that there is a second release of active agent. The release rate of the “secondary burst” of the instant claims is defined as occurring over 2-4 days in the specification (specification p15, lines 10-12) and therefore the second release of active agent of Krone et al. encompasses the “secondary burst” of the instant claims as it may be a prolonged release.

26. In regards to the “lag time” the specification recites (p13, lines 17-20 and 30-33), “a secondary “lag phase” of **low or no** release of the drug followed by a second burst”. Therefore, the polytartrate tablet formulations which are prepared via compaction/compression of Krone et al. encompass the composition of the instant claims as they have a first “initial burst”, an implied second release of active agent (burst) and the phase between the bursts (i.e. lag phase) which may release drug. Therefore, the time between bursts of the polytartrate formulations of Krone et al. encompass the “lag phase” of the instant claims.

27. The standard compression force for the preparation of a conventional tablet is in the range of 18 to 27 kN as taught by Lewis and therefore the polytartrate solid tablets (prepared via compression), which do not comprise a barrier structure, of Krone et al. encompass the composition of the instant claims which is prepared via compression with a compression force from 10 to 65 kN/cm². The simple compression of polytartrate compositions provides for release of the pharmaceutically active material in a pulsatile manner as evidenced by the specification (specification p3, lines 28-33). Krone et al.

Art Unit: 1618

does not explicitly teach that the tablets are pulsatile but teaches that the polytartrate composition are prepared via compression and have a decreased "initial burst" which shows that they provide an initial burst and thus are pulsatile to a degree.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

28. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

29. Claims 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Krone et al. (US 5,391,696).

30. Krone et al. (US 5,391,696) teaches of formulations comprising a.) polytartrate polymer, such as (2',3'-(1',4'-diethyl)-L-tartyl poly-(2,3-O-isopropylidene)-L-tartrate); b.) buserelin; c.) polyethylene glycol and d.) pharmaceutically acceptable excipients, etc. (abstract; column 10, lines 36-45 and 54-59) as well as that stated above.

31. The polytartrate formulation of Krone et al. anticipates the pharmaceutical composition of the instant claims and is capable of the same functions, such as releasing the pharmaceutically active material in a pulstile manner including an initial burst, a lag phase, and thereafter a secondary burst when the pharmaceutical composition is orally administered to a human or animal and have the same properties.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618